PREFACE

Our understanding of the processes underlying the pathogenesis of neoplastic and nonneoplastic lung disease from particle exposure has advanced rapidly in recent years. In addition, significant progress is being made on defining the molecular mechanisms by which particles interact with different lung cell populations to elicit responses. The Sixth International Meeting on the Toxicology of Natural and Man-Made Fibrous and Non-Fibrous Particles is part of a meeting series initiated in 1978, at the Medical Research Council Unit in Cardiff, Wales. All of the meetings in this series have been organized to provide a forum for discussion and debate on recent scientific findings and concepts on the toxicology of particles.

The Sixth International Meeting was held 15–18 September 1996 in Lake Placid, New York. The meeting was attended by 240 academic, government, and industry scientists from 18 different countries. Meeting sessions were organized on several topic areas including: physical and chemical properties of particles; molecular mechanisms of carcinogenesis; intracellular signaling; oxidative stress; cytokines; and regulatory issues. A number of reoccurring themes were noted. For example, in several of the sessions, the topics of transition metals, redox cycling and oxidative stress were discussed as key factors in response to mineral dusts and ambient fine particulate air pollution. Evidence was presented by several scientists that transition metals at high doses can contribute to the genotoxic, cytotoxic, and *in vivo* inflammatory activity of various particulate materials. Also, presentations focused on the emerging role of oxidants in the process of cell activation, particularly in the regulation of genes associated with inflammatory and immune responses. Another recurrent issue raised was species differences in response and, in particular, mechanisms underlying these differences and the impact on the hazard evaluation and risk assessment process. Several platform and poster presentations reported on differences in cytokine and oxidant production as well as cell activation pathways that may contribute to species differences in particle toxicity. In the areas of carcinogenesis and cell signaling, from the many presentations on these topics, it was clear that considerable progress is being made in determining the molecular processes underlying how lung cells responsed to fibrous and nonfibrous particles. Of particular note were presentations on cell cycle regulatory genes in epithelial and mesothelial cells and activation of specific cell membrane receptors and associated signaling pathways. Regarding regulatory issues, the appropriate design and interpretation of particle toxicology studies was a key theme. The difficulties of defining maximum tolerated dose for particulate inhalation studies were discussed and some potential alternatives to the traditional approaches proposed. The question of the rat as a model for assessing carcinogenic hazards to humans was reviewed under the aspect that the rat lung appears very sensitive of certain poorly soluble particulate materials. Other concepts echoed throughout the meeting were the need for thorough characterization of test particles and, wherever possible, *in vivo* confirmation of *in vitro* mechanistic findings.

The meeting was successful in providing a forum for presentation and discussion of some of the latest research on the toxicology of natural and man-made particles. We are very grateful to the members of the International Advisory Committee and the members of the Local Organizing and Scientific Committee for helping to make this meeting a success. We would also like to thank the companies and organizations whose names are listed on the title page for their sponsorship and generous financial support of this meeting. Special thanks are due to the members of the Editorial Committee, acknowledged at the end of the proceedings, for their rigorous peer-review of the submitted manuscripts. The next meeting in this series will be held in Maastricht, The Netherlands, and is tentatively scheduled for fall 1999. Drs. Paul Borm and Ken Donaldson will be the co-organizers of the next meeting.

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